REMARKS/ARGUMENTS

This Amendment addresses the issues raised in the Official Action of March 27, 2008, a Final Rejection. Claims 1-17 are pending in the application of which claims 1, 2 and 11 are examined on the merits and are rejected. The remaining claims 5-10 and 12-17 have been withdrawn from consideration as directed to non-elected subject matter.

Claims 5-10, all withdrawn claims, are above amended and directed to methods of treatment. These claims depend directly or indirectly from claim 1 thus applicants request rejoinder of these claims once allowable subject matter is indicated.

As a consequence of these amendments claims 3-4 have been canceled. Claims 1 and 2 are amended as discussed below.

Responsive to the examiner's requirement on page 2 of the Official Action, submitted herewith is a verified English translation of the priority document.

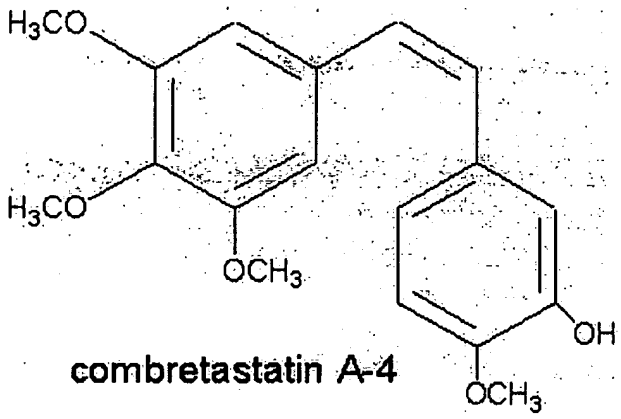
The examiner's comments in item 1 of the Official Action have been considered and claim 1 has been amended to clarify the meaning of R_1, R_2, R_3, and R_4 rendering this rejection moot.

Responsive to item 6 of the Official Action, claims 1 and 2 have been amended and restricted to elected subject matter.

This leaves for consideration the rejection of amended claims 1 and 11 as being "obvious" and therefore unpatentable over U.S. 5,858,955 to Kawai et al.

Kawai et al describe a class of compounds that are known to persons skilled in this field as combretastatin derivatives The examiner argues that the teaching of Kawai et al of treating bone disorder makes the present invention obvious.

Applicants respectfully disagree with the examiner since the present invention gives an additional feature which was not derivable from the prior art. In fact, on page 57 the present inventors report that it is known in the prior art that combretastatin derivatives, as A4-P, have side effects and show dose-limiting toxicity (Cancer Res., 62:3408-3416, 2002).



combretastatin A-4

Starting from this point, the present inventors studied the effect of ST2496 (the elected species) and other compounds on cardiovascular parameters.

ST2496 and Combretastatin A4 were injected in the jugular vein of Wistar rats at the doses of 20 or 40 mg/kg in order to consider blood pressure and heart rate. The results in Figure 1 show that Combretastatin A4 induces increase in blood pressure and a progressive decrease of heart rate, while ST2496 did not show significant effect on the parameter considered.

The unexpected properties that the claimed compounds avoid these effects on the cardiovascular system and show reduced toxicity would not be expected by the skilled person since the prior art is completely silent on this problem. This is of particular significance to the (withdrawn) method of treatment claims 5-10.

The results shown in the present application are unexpected to the skilled person and unpredictable from the teachings given by Kawai et al. In fact, Kawai et al present only preparation examples and do not report any working example on the pharmacological characteristics of their compounds.

The distinguishing feature of present compounds, namely the presence of a phosphate ester, is hardly derivable from Kawai et al, also because the similarity between the side groups on the furan ring which suggest that structural similarity implies similar properties. The results present in the application disprove the above expectation.

Therefore, claims 1, 2 and 11 are inventive over the prior art because they are less toxic and avoid side effects on the cardiovascular system and the skilled person would not be able to

derive said essential feature directly and unambiguously from the prior art without exercising additional skills.

In view of the above applicants request the withdrawal of the obviousness rejection.

Respectfully submitted,

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